IBMTR/ABMTR Mortimer M. Bortin Awards for Outstanding Research in Bone Marrow Transplantation

Mortimer M. Bortin, M.D., was one of the founding members of the IBMTR and served as its Scientific Director for more than 30 years. The Mortimer M. Bortin Award, established to commemorate Dr. Bortin's contribution to the field of transplantation, is presented each year to one or more investigators submitting abstracts for presentation at the annual IBMTR/ABMTR meeting. The abstracts must address important issues in experimental or clinical blood and marrow transplantation and be deemed to be of outstanding scientific merit.

This year, three $1,000 awards will be presented on behalf of the Mortimer M. Bortin Fund Awards Committee. The awards are supported by an educational grant from Gambro BCT, Inc.

NO DELETERIOUS EFFECT OF HLA-MISMATCHING OUTSIDE CROSS REACTIVE GROUPS (CREG) COMPARED TO WITHIN CREG MISMATCHES FOLLOWING UNRELATED DONOR BONE MARROW TRANSPLANT

Wade, J.A.[2]; Takemoto, S.K.[3]; Thompson, J.[4]; Hurley, C.K.[5]; Fuller, T.C.[6]; Rodey, G.[7]; Davies, S.M.[8]; Confer, D.L.[1]; Kollman, C.[1] 1. National Marrow Donor Program, Minneapolis, MN; 2. University of Toronto, Toronto, ON, Canada; 3. UCLA Dept. of Pathology, Los Angeles, CA; 4. University of Kentucky, Lexington, KY; 5. Georgetown University, Washington, DC; 6. University of Utah, Salt Lake City, UT; 7. Baylor College of Medicine, Houston, TX; 8. University of Minnesota, Minneapolis, MN

Strategies for selecting a partially HLA-mismatched donor vary when a full match cannot be identified. Some transplant centers have limited donor selection to mismatches within an HLA-A or HLA-B CREG. HLA antigens within a CREG share polymorphic sequences which form public epitopes identified by alloantisera.

To assess whether an HLA mismatch within a CREG group ("minor") may result in better outcome than a mismatch outside CREG groups ("major"), we analyzed validated outcomes data from 6931 transplants facilitated between 1987 and 1999 by the National Marrow Donor Program. Of these cases, 1175 (17%) were HLA-DR matched but had an antigen level mismatch at HLA-A or B. Mismatches within a CREG were deemed "minor" using three published CREG matching schemes.

Univariate analyses (Kaplan-Meier for survival and cumulative incidence for the other outcomes) suggest that outcome is not significantly different between "minor" and "major" mismatches. The table gives a comparison of outcomes with 95% confidence interval among the subset of HLA-DRB1 allele matched pairs (N = 5181).

Multivariate analyses on all 6931 cases adjusting for diagnosis, transplant center, HLA-DRB1 matching and other relevant risk factors confirmed these results. HLA-A,B matched cases had significantly better outcome than mismatched ("minor" or "major") cases, but there were no detectable differences between "major" and "minor" mismatches. This provides a larger acceptable pool of donors for patients without a perfect match.

Outcome	HLA–A,B Matched	"Minor" Mismatch	"Major" Mismatch
Engraftment	96% ± 1%	93% ± 2%	91% ± 3%
Grades II–IV aGvHD	48% ± 1%	53% ± 4%	53% ± 6%
Grades III–IV aGvHD	30% ± 1%	36% ± 4%	38% ± 5%
Chronic GvHD (2 yrs)	49% ± 2%	45% ± 5%	48% ± 7%
Survival (5 yrs)	33% ± 2%	20% ± 5%	21% ± 5%

PERIPHERAL STEM CELLS VERSUS BONE MARROW FROM UNRELATED DONORS. A MATCH PAIR ANALYSIS OF 214 PATIENTS

Ringdén, O.[1]; Remberger, M.[1]; Blau, I.[3]; Ottinger, H.[2]; Kiehl, M.[3]; Aschan, J.[1]; Beelen, D.[2]; Basara, N.[3]; Fauser, A.[3]; Runde, V.[2] 1. Huddinge University Hospital, Stockholm, Sweden; 2. BMT Unit, Essen, Germany; 3. BMT Unit, Idar-Oberstein, Germany

The clinical results between 107 patients receiving a G-CSF mobilised peripheral blood stem cell graft (PBSC) graft from an HLA-A, -B and -DR compatible unrelated donor were compared to 107 matched controls receiving an unrelated bone marrow (BM) transplant. Engraftment was achieved in 94% of the patients in both the PBSC and the BM group. The PBSC graft contained significantly more nucleated cells, CD34+, CD3+ and CD56+ cells ($p<0.001$) and resulted in a significantly shorter time to neutrophile (15 vs 19 days) and platelet engraftment (20 vs 27 days) compared to the BM control group ($p<0.001$). Probability of acute GVHD II-IV were 35% and 32% (ns), and probability of chronic GVHD were 61% and 76% (ns), in the PBSC and BM groups, respectively. There was no difference in bacteraemia, CMV reactivation, CMV disease and fungal infection between the two groups. Three years transplant related mortality (TRM) was 42% in the PBSC group and 31% in the BM controls (ns) and survival was 46% and 45%, respectively. Among patients with a malignant disease, probability of relapse was 25% and 31% in the two groups, respectively (ns), resulting in a disease-free survival of 43% in the PBSC group and 46% in the BM controls (ns). In multivariate analysis early disease, acute GVHD 0-I and presence of chronic GVHD were independent factors associated with a better disease-free survival in this study.

Conclusion: PBSC from HLA-compatible unrelated donors gives faster engraftment compared to bone marrow, but has otherwise a similar outcome.

IMMUNITY OF PATIENTS SURVIVING 20-30 YEARS AFTER ALLOGENEIC OR SYNGENEIC BONE MARROW TRANSPLANTATION

Storek, J.[1]; Espino, G.[1]; Douek, D.C.[2]; Dawson, M.A.[1]; Hill, B.[2]; Mary, F.E.[1]; Martin, P.[1]; Maloney, D.G.[1] 1. Fred Hutchinson Cancer Research Center, Seattle, WA; 2. University of Texas Southwestern Medical Center, Dallas, TX

Background. The duration of immunodeficiency following marrow transplantation is not known.

Methods. Using questionnaires, we studied the infection rates in 72 patients surviving 20-30 years after allogeneic or syngeneic marrow grafting. Furthermore, in 33 of the 72 patients and in 16 donors (siblings who originally donated the marrow) leukocyte subsets were assessed by flow cytometry. T cell receptor excision circles (TREC), markers of T cells generated de novo (from hematolymphopoietic cells), were quantitated by real-time PCR. IgG2 and antigen-specific IgG levels were determined by ELISA.

Results. Infections diagnosed after 15 years posttransplant occurred rarely. The average rate was 0.07 infections per patient-year or one infection every 14 years, excluding respiratory tract infections, gastroenteritis, lip sores and hepatitis C. The counts of monocytes, NK cells, B cells, total CD4 T cells and total CD8 T cells in the patients were not lower than in the donors. The counts of phenotypically naïve CD4 T cells and TREC+ CD4 T cells in patients transplanted before the age of 18 years were similar to the counts in their donors. These were approximately 50% lower in patients transplanted at the age of ≥18 years compared to their donors. The levels of total IgG2 and specific IgG against Haemophilus influenzae and Streptococcus pneumoniae were similar in patients and donors.

Conclusion. Overall, the immunity of patients surviving 20-30 years posttransplant is normal or near-normal. There appears to be a minor, clinically insignificant deficiency of naïve CD4 T cells in patients who were transplanted at age ≥18 but not in those who were transplanted at age <18.